ינואר 2022

רופא/ה נכבד/ה, רוקח/ת נכבד/ה,

<u>הנדון: עדכון העלון לרופא של התכשירים:</u>
<u>Mayzent 0.25 mg: 165-54-36195</u>
<u>Mayzent 2 mg: 165-55-36196</u>

התכשירים שבנדון רשומים בישראל להתוויות הבאות:

Mayzent is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease, and active secondary progressive disease, in adults.

המרכיב הפעיל:

Siponimod (as Fumaric Acid) 0.25 mg and 2 mg

ברצוננו להודיעכם על עדכונים בעלון לרופא של התכשירים בנדון.

בהמשך המכתב מפורטים השינויים המהותיים בלבד (ללא שינויי נוסח, עריכה, אדמיניסטרציה וכו').
שינויים אשר מהווים החמרה מסומנים עם רקע צהוב.

העלון לרופא המעודכן נשלח למאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על-ידי פניה לבעל הרישום.

בברכה,
סיון לידאני ברג
רוקחת ממונה

Novartis Israel Ltd.
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שינויים בעלון לרופא

4.5 Interaction with other medicinal products and other

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Vaccination

The use of live attenuated vaccines may carry the risk of infection and should therefore be avoided during siponimod treatment and for up to 4 weeks after treatment (see section 4.4).

During and for up to 4 weeks after treatment with siponimod vaccinations may be less effective. The efficacy of vaccination is not considered to be compromised if siponimod treatment is paused 1 week prior to vaccination until 4 weeks after vaccination. In a dedicated phase I healthy volunteer study, concomitant siponimod treatment with influenza vaccines or shorter treatment pause (from 10 days prior to 14 days after vaccination) showed inferior responder rates (approximately 15% to 30% lower) compared to placebo, while the efficacy of a PPV 23 vaccination was not compromised by concomitant siponimod treatment (see section 4.4).

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CYP2C9 and CYP3A4 inhibitors

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The co-administration of fluconazole (moderate CYP2C9/~~strong~~ CYP3A4 dual inhibitor) 200 mg daily at steady state and a single dose of siponimod 4 mg in healthy volunteers with a CYP2C9*1*1 genotype led to a 2-fold increase in the area under the curve (AUC) of siponimod.

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CYP2C9 and CYP3A4 inducers

Siponimod may be combined with most types of CYP2C9 and CYP3A4 inducers. However, because of an expected reduction in siponimod exposure, the appropriateness and possible benefit of the treatment should be considered when siponimod is combined:

- with strong CYP3A4/moderate CYP2C9 dual inducers (e.g. carbamazepine) or a moderate CYP2C9 inducer in combination with a separate strong CYP3A4 inducer in all patients regardless of genotype
- with moderate CYP3A4 inducers (e.g. modafinil) or strong CYP3A4 inducers in patients with a CYP2C9*1*3 or *2*3 genotype.

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5.2 Pharmacokinetic properties

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Characteristics in specific groups or special populations

CYP2C9 genotype

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There are other less frequent occurring polymorphisms for CYP2C9. The pharmacokinetics of siponimod have not been evaluated in such subjects. Some polymorphisms such as *5, *6, *8 and *11 are associated with decreased or loss of enzyme function. It is estimated that CYP2C9 *5, *6, *8 and *11 alleles have a combined frequency of approximately 10% in populations with African ancestry, 2% in Latinos/Hispanics and <0.4% in Caucasians and Asians.

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